ON THE ACTIVE PRINCIPLE OF RHUS TOXICODENDRON AND RHUS VENENATA

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Plate X.

Of all the cutaneous eruptions caused accidentally by vegetable matters, that produced by the different kinds of Rhus is probably the most common in this country. The common occurrence of poisoning with poison ivy and poison sumach, and the lack of any rational treatment for this, led me to try to isolate the active principle of these plants, in the hope that a knowledge of its characteristic properties might serve as the basis for such treatment.

It is, as is well known, the general belief of the public and of most physicians that the eczematous conditions which occur in many persons after handling such plants may be caused also by emanations from the plant, the active principle being thought to be a volatile substance. The two previous attempts which have been made to isolate the poisonous principle failed. Nevertheless the investigators making them shared the general opinion that the active substance is volatile.

The first who attempted to isolate the active principle of Rhus toxicodendron was J. Khittel.* He attributed the action of poison ivy to a volatile alkaloid.

Later, in 1865, John M. Maisch published† a preliminary notice "On the Active Principle of Rhus toxicodendron." He could not agree with Khittel's statements and denied the presence of a volatile alkaloid. He thought that he had found a new volatile acid, which he held to be the active principle and which he called toxicodendric acid.

As Maisch's article is the only paper which is now quoted when one

* Wittstein's *Vierteljahresschrift für praktische Pharmacie*, vii, 348–359, 1858.
† *Proceedings of the American Pharmaceutical Association*, 1865, 166.

speaks of the active principle of Rhus, I may be allowed a few remarks upon it. After having failed to obtain the volatile alkaloid of which J. Khittel spoke, Maisch performed the following experiment. He enclosed in a tin box a lot of freshly collected leaves of poison ivy, and introduced into this box a number of moistened test papers. The next morning he found that the blue litmus paper had been colored strongly red, whereas curcuma and red litmus paper were unaffected. He writes regarding this experiment: "This single experiment was at once a conclusive proof that the exhalations of these leaves contained a volatile acid, and that the poisonous properties were most likely due to it." Maisch describes further how he obtained an impure watery solution of his toxicodendric acid by maceration of the leaves, expression and distillation of the expressed liquid. In preparing his acid, Maisch suffered from a copious eruption and the formation of numerous vesicles on the back of his hands, fingers, wrists and bare arms. He says further: "Several persons coming into the room while I was engaged with it were more or less poisoned by the vapors diffused in the room, and I even transferred the poisonous effects to some other persons merely by shaking hands with them. The dilute acid, as obtained by me, and stronger solutions of its salts, were applied to several persons, and eruptions were produced in several instances, probably by the former, though not always, which was most likely owing to the dilute state of the acid."

Maisch did not isolate his acid nor any one of its salts; he never had the substance in question chemically pure. He concludes his article with the following words: "Even in the chemical history of this acid, nearly everything is to be found out yet by further researches. If my time permits I may attempt to prepare it in larger quantities and in a more concentrated form, and to determine its composition." No further publication by Maisch or by any other investigator has appeared.

Maisch's view has been generally held to be correct and his toxicodendric acid has been accepted as the active principle. We find his article quoted by Husemann.* Lewin† mentions toxicodendric acid

* Aug. Husemann, A. Hilger und Theod. Husemann, Die Pflanzenstoffe, 2te Aufl., 867.

† L. Lewin, Die Nebenwirkungen der Arzneimittel, 766.

as the probable active principle. In the U. S. Dispensatory and by Dr. James C. White,* the toxicodendric acid of Maisch is recognized as the active principle of Rhus, and speculations are made as to what should be the treatment of the dermatitis caused by this acid. But Husemann† remarks that Buchheim held the active principle of Rhus to be cardol, and Schmiedeberg‡ and Boehm§ quote Buchheim's supposition without mentioning the toxicodendric acid at all.

As has been stated, Maisch never isolated his toxicodendric acid in a chemically pure state. He proved only the presence of a volatile acid. He further noticed the characteristic eruption on his own skin while he was working with the poison ivy. Persons coming to the laboratory at this time were often poisoned there. He observed also that an eruption sometimes followed the application of the impure solution of this acid to the skin. From these very rudimentary experiments he draws the wholly unwarranted conclusion that his acid must be the active principle.

To demonstrate the pharmacological actions of any one substance, the first thing necessary is to have this particular substance chemically pure. Experiments made with impure substances have only a very restricted value, if any, and can never be conclusive as to the real nature of a substance and its properties. Whether Maisch's toxicodendric acid, or any other substance, is the active principle of Rhus can be decided only by preparing these substances chemically pure and studying their action.

Before describing the methods of isolation and purification of the different substances obtained from poison ivy and poison sumach, I wish to state in a few words the classification of the different cutaneous irritants as given by Schmiedeberg.|| According to this author, all skin irritants may be divided into three different groups. In the first or " turpentine group " are comprised all substances which at ordinary temperature are not too difficultly volatile. To this group belong the

* James C. White, Dermatitis venenata. Boston, 1887.
† Loc. cit.
‡ O. Schmiedeberg, Grundriss der Arzneimittellehre, 3te Aufl., 1895, 222.
§ R. Boehm, Lehrbuch der Arzneiverordnungslehre, 2te Aufl., 1891, 374.
|| Op. cit., 213–224.

different turpentines, many ethereal oils of the vegetable kingdom, many substances of the fatty series of organic compounds, and also aromatic compounds like benzol, etc. The more volatile a substance, the quicker its action; formic and acetic acids, for example, act more quickly than the less volatile acids of the same series.

If substances which are volatile have in addition a very stimulating action upon the skin, as is seen in a very high degree in the case of mustard oil, their action will be a very vigorous one. They produce in a very short time all degrees of general stimulation: pain, redness of the skin, exudative inflammation with formation of bullæ, formation of pus and necrosis of the tissue. The second group of skin irritants is represented according to Schmiedeberg specially by mustard oil.

In the third group of skin irritants are classed by the same author all substances which have a specific irritant action upon the skin, but which are not volatile at ordinary temperature. Their action will be slower than the substances of the preceding groups, and as a rule less vigorous.

This is the only scientific classification of cutaneous irritants that has been made, as far as I know, and all substances known to us as such irritants can easily be brought into one of the three groups according to their action.

Without knowing the real active principle of Rhus, the clinical history of the dermatitis caused by the unknown substance leads one necessarily to suppose that the poisonous substance should belong to Schmiedeberg's third group of skin irritants, that is to say, it ought to be a non-volatile specific skin irritant. Of course only experiments with the isolated and pure substance can settle this question definitely.

I will now briefly describe my own experiments. My first endeavor was to get Maisch's acid pure and to determine its composition.

An aqueous solution of Maisch's acid was easily obtained by distilling the finely divided fresh plant in a current of steam. By previously acidulating with dilute H_2SO_4 the yield of Maisch's acid was considerably increased. The addition of H_2SO_4 did not alter the nature of the acid, as was proved by separate distillation of the drug without

the use of H_2SO_4. The distillate, which showed strongly acid reaction, after neutralization with an alkali left on evaporation the corresponding salt. In this way the barium and sodium salts were prepared. After repeated crystallization from dilute alcohol the salts were secured chemically pure, as was shown by the analyses of the products of different preparations.

The acid distillate, which, as already noticed by Maisch, had a peculiar odor, contained besides the acid, traces of an oil, which could be separated from the solution by shaking it with ether. The ethereal solution left on spontaneous evaporation a very small amount of an oily substance with quite an agreeable odor. To this oil we shall refer later.

The crystallization of the impure barium salt of Maisch's toxicodendric acid was accomplished by dissolving the salt in water, heating the solution nearly to the boiling point and adding alcohol until a faint cloudiness appeared. The glass was now covered and set aside. On cooling, long crystals appeared, which sometimes were over 1 cm. long. The sodium salt was obtained in beautiful white crystals, often 2 and 3 cm. long. The latter salt was deliquescent. Both salts were very easily soluble in water.

The analyses of the salts of different preparations gave the following results:

ANALYSES OF THE BARIUM SALT.

I. Barium salt, air-dry, 0.9750 gramme lost on heating 0.0620 gramme H_2O, and gave on ignition with H_2SO_4, 0.8378 gramme $BaSO_4$.

II. 0.5440 gramme barium salt (of the same preparation) lost by 110° C. 0.0353 gramme H_2O, and gave 0.4670 gramme $BaSO_4$.

III. 0.5800 gramme (of the same preparation as used in analyses I and II) lost 0.0380 gramme H_2O at 110° C. The dried substance gave 0.2773 gramme CO_2 and 0.4215 gramme $BaCO_3$. The water was lost in this analysis.

IV. 0.5340 gramme of the same substance lost at 110° C. 0.0350 gramme H_2O, and gave 0.1198 gramme H_2O, 0.2535 gramme CO_2, and 0.3879 gramme $BaCO_3$.

V. 0.4586 gramme substance of another preparation, dried at 105–110° C., gave 0.1178 gramme H_2O, 0.2303 gramme CO_2, and 0.3573 gramme $BaCO_3$.

VI. 0.3465 gramme of a third preparation gave 0.0221 gramme H_2O and 0.2969 gramme $BaSO_4$.

ANALYSES OF THE SODIUM SALT.

I. 0.4715 gramme air-dry substance lost on heating to 105–110° C. 0.1875 gramme H_2O, and gave on ignition with H_2SO_4, 0.2450 gramme Na_2SO_4.

II. 0.6430 gramme lost on heating to 105–110° C. 0.2558 gramme H_2O, and gave on ignition with H_2SO_4, 0.3370 gramme Na_2SO_4.

III. 0.7092 gramme lost 0.2830 gramme H_2O by 105° C., and gave on ignition with H_2SO_4, 0.3677 gramme Na_2SO_4.

BARIUM SALT.

Water Found					Calculated for
I.	II.	III.	IV.	VI.	$Ba(C_2H_3O_2)_2 + H_2O$.
6.36	6.49	6.56	6.55	6.39	6.59 per cent H_2O

	Found						Calculated for
	I.	II.	III.	IV.	V.	VI.	$Ba(C_2H_3O_2)_2$.
Ba,	53.95	53.96	54.08	54.07	54.18	53.84	53.71
C,			18.69	18.58	18.45		18.83
H,			*	2.66	2.85		2.35

SODIUM SALT.

Water Found			Calculated for
I.	II.	III.	$NaC_2H_3O_2 + 3H_2O$.
39.76	39.78	39.90	39.71 per cent H_2O

Sodium Found			Calculated for
I.	II.	III.	$NaC_2H_3O_2$.
27.95	28.17	27.94	28.05 per cent Na

On heating one of the salts with sulphuric acid and alcohol the characteristic odor of acetic ether was developed. The watery solution of the alkaline salt gave, on addition of ferric chloride, a blood-red color. In short, Maisch's toxicodendric acid proved to be nothing but acetic acid, and was therefore not the real cause of the peculiar dermatitis caused by poison ivy.

The real active principle of the Rhus plants was obtained in an impure state by extracting the plant with alcohol, distilling off the alcohol, washing the black, oily residue with water and taking it up in ether. The ethereal solution was then first washed with water and with dilute solution of sodium carbonate and again with water. By evaporating the ether an oily substance of very dark color was obtained, and this when applied to the human skin showed the well-known lesions occurring after contact with some part of the Rhus plant.

This oil was far from being a pure substance, as could be easily seen by simply treating it with alcohol. One part of it dissolved

* The determination of H_2O in this analysis was lost.

easily in this vehicle, leaving a residue which was soluble with difficulty even in warm alcohol. The isolation and purification of the active principle from this oily mixture offered some difficulties. The process finally adopted was the following: The oily mixture was treated with 10 to 15 times its bulk of 95 per cent alcohol at ordinary temperature. The alcoholic solution, decanted from an insoluble resinous residue, deposited on standing more of the resinous matter taken up by it. After standing two days the alcoholic solution was filtered and an alcoholic solution of lead acetate was added to it. The precipitate formed was of a very dark color, and was not the pure lead compound of the oily active principle, for the obtaining of which fractional precipitation had to be resorted to. The later precipitates so obtained consisted of the lead compound of the oil in a pure state. The first precipitates were contaminated with the resinous material referred to above. From the filtrate of these lead precipitates another oil was obtained by getting rid of the excess of lead with ammonium sulphide, diluting with water and shaking with ether. On allowing the ether to evaporate spontaneously, an oil with an agreeable odor was obtained. This oil seemed to be identical with that obtained in small quantity in the distillation of the finely divided plant in a current of steam. This oil apparently had no irritant action upon the skin.

The free active oil was separated from its uncontaminated lead compound, obtained as just described, by decomposition with ammonium sulphide and gave the characteristic skin eruptions. The purity of the lead compound of the oil was demonstrated by quantitative analyses of two different preparations, one from the fruit of Rhus toxicodendron and the other from the leaves; the plants having been collected at different seasons and in different localities.

I. 0.2563 gramme lead compound (dried at 105° C.) gave 0.1406 gramme $PbSO_4$.

II. 0.2192 gramme of the same preparation gave 0.1106 gramme H_2O and 0.3610 gramme CO_2.

III. 0.3001 gramme (of another preparation) gave 0.1640 gramme $PbSO_4$.

IV. 0.2400 gramme gave 0.1152 gramme H_2O and 0.3949 gramme CO_2.

	Found				Calculated for $C_{21}H_{30}O_4Pb$.
	I.	II.	III.	IV.	
Pb,	37.49		37.32		37.43
H,		5.61		5.33	5.42
C,		44.94		44.88	45.56

The free oil obtained from the pure lead compound has as yet not been analysed.*

For this poisonous oil, which is not cardol, from which it differs in chemical properties, I propose the name of Toxicodendrol. It was found in all parts of the plant—in the stems, branches, roots, leaves and fruit—its amount, however, varying, the fruit and leaves containing most. The oil was found in Rhus toxicodendron as well as in Rhus venenata. We were not able to find any essential difference between the oil obtained from the two different species. Rhus venenata seemed to contain more oil than Rhus toxicodendron.

A few quantitative estimations were made of the crude oil, that is to say, the mixture of the active oil contaminated with the resinous matter and the oil not giving a lead precipitate. It was found that the leaves of Rhus toxicodendron contained 3.3 per cent crude oil, whereas the fruit contained 3.6 per cent, and the stems and branches of the same plant only 1.6 per cent. The oil obtained from the fruit seemed to be the purest; the one from the leaves, and especially from the branches, containing more resinous matter.

Toxicodendrol is easily soluble in alcohol, ether, benzol, chloroform, etc., but is insoluble in water. Toxicodendrol is decomposed easily by heat, but only slowly at ordinary temperature. A sample of it, which had been left for thirteen months in an open porcelain dish, was partly converted into a resin, but the remaining oil proved to be just as active as before.

The active oil was prepared also from plants which had been collected during the winter, after being covered with snow for weeks. Old stems and branches of the plant which had been kept in the laboratory over a year and were perfectly dry gave still quite a considerable amount of active oil. The only difference between the fresh and the

* The results as published here were obtained by me more than a year ago. Through other work, my time has been taken up so that I could not proceed further. This research is now being continued in the laboratory. We shall first prepare other derivatives of the oil to establish a definite molecular formula, and further, we shall compare more accurately the two oils obtained from Rhus venenata and Rhus toxicodendron, to see whether they are really identical or not.

old plant was that the former was less contaminated with resinous matter.

The action of the oil isolated from Rhus toxicodendron seemed to be identical as to kind and intensity of action with that from Rhus venenata. Clinical observation had established long before that the dermatitis caused by either plant is identical in appearance. Poison sumach was thought to be only a stronger poison. Should both poisons even in final tests prove to be identical, the difference in the strength of the action of poison ivy and of poison sumach would be easily explained by the fact that the latter contains more of the active oil.

As an example of the effect of the isolated oil upon the human skin, I shall describe a case of poisoning with the oil from Rhus venenata. I relate this case not because the oil used was from Rhus venenata, but because the person upon whom the experiment was performed, Dr. Cleon Melville Hibbard, was in former years often accidentally poisoned in a severe manner when handling poison oak or poison sumach. Furthermore, Dr. Hibbard was extremely interested in this question and was self-sacrificing enough not only to be the subject of the experiment, but also to take minute notes of the progress of the experiment and to have the affected parts photographed twice.

The following extract is taken from his notes:

"1894, October 13, 5 P. M. On the anterior surface of the left forearm, three inches from the wrist, some of the oil extracted from Rhus venenata was placed with a glass rod. The forearm was then wrapped with absorbent cotton and bandaged.

11 P. M. Left forearm had a very slight burning sensation. An area the size of a cent about the point of application of the oil was reddened. New dressing put on.

Oct. 14, 7 A. M. Burning sensation slightly increased. The area which was inflamed last night has now about 10 vesicles dotted over it, and the redness has increased to the size of a dollar.—P. M. The area of inflammation now about 1½ inches in diameter. The vesicles seen in the morning have become confluent and appear as one large blister the size of a ten cent piece.

Oct. 15, 7 A. M. The left forearm itched considerably during the night. Redness now 2 inches in diameter and becoming somewhat

swollen.—P. M. The arm is now considerably swollen and slightly painful.

Oct. 16, 7 A. M. Arm more painful and tender. The photograph taken this A. M. (Plate X, Fig. 1) gives a good idea of the distribution of the vesicles and the degree of swelling. Applied a paste of zinc oxide ʒss, amyli, vaseline āā ʒss at 12 M. and again at 7 P. M.

7 P. M. The vesicles are larger and redder than this A. M. There are a few (6 or 7) vesicles on index finger and a few scattered all around the forearm.

9 P. M. Swelling extends now from knuckles to the elbow. Pronation and supination painful, feels very uncomfortable. Paste used with light bandage, instead of the heavy bandage of absorbent cotton as heretofore.

Oct. 18, A. M. Blisters began to break down yesterday and considerable watery fluid ran from the arm. Dressed the arm several times with the above-named paste. Last night applied a mixture of 2 per cent carbolic vaseline and boracic acid ointment. The swelling extends now from between the fingers to above the elbow. The area first affected does not look so red now, nor is it so tender as yesterday. On the edge new vesicles are coming out. The whole arm throbs and burns considerably.

11 P. M. Removed the point of infection, an area 1 inch by $\frac{3}{4}$ inch which had become black and necrotic; it was about $\frac{1}{8}$ inch in depth. Arm dressed with carbolic vaseline.

Oct. 19, 10 A. M. Arm is considerably swollen to 5 inches above elbow, and some small vesicles here are quite visible. The extent of the swelling can be seen from the second photograph (Plate X, Fig. 2), which is blurred somewhat with the zinc paste. Yet it can be seen that even the finger-joints were noticeably swollen. The whole arm has been oozing since the 17th, and required dressing several times a day. The vesicles are now becoming confluent and form blisters the size of a dollar all over the arm.

Two days ago two small blisters appeared on the index finger of the right hand; they have been washed most thoroughly with soap and water and the scrubbing brush, and have not spread much in the last 24 hours. During the daytime have carried the arm in a sling since the 16th of October. At night supported arm on a pillow outside of the sheets and blankets, with only an ointment bandage covering it.

Oct. 20, at Dr. Pfaff's suggestion, I stopped applying any ointment and began to scrub the whole arm with soap and water. Although it burned some when rubbed, it was not very painful, and the relief obtained from such treatment was as soothing as after applying the carbolic vaseline.

The arm was treated thus several times a day. Went in town to-day, and as it was painful to bend the elbow, I did not carry the arm in a sling; as a result of this and the car ride, the œdema of the arm became very great, and this caused considerable pain. Supporting it upon a table while sitting in a low chair for several hours gave much comfort and caused an œdematous swelling to collect in the axilla, which disappeared the next day. The vesicular eruption is now at a standstill.

Oct. 23. From Oct. 21st the swelling gradually disappeared, and to-day arm is back to normal size. The blebs continued to fill with serum in places until to-day, the parts first affected drying up 3 or 4 days ago. An interesting point is that from the time that water and the scrubbing brush were used, and the ointment stopped, the spreading also stopped, and it left patches on the back of the hand unaffected.

At the height of the inflammation in the arm an intense pruritus ani started up, but 2 or 3 days treatment with soap and water caused it to disappear.

Oct. 27. After Oct. 23 desquamation began, and by to-day this process is complete. Now new tissue covers the whole surface that was covered with blisters. The time taken for the healing of the arm from the beginning of the inoculation was just two weeks. There were never any general symptoms, excepting one day a slight fever."

Dr. Hibbard's case ran the ordinary course of a severe dermatitis caused by poison ivy or poison sumach, and as we find so well described by Dr. J. C. White.* The photographs accompanying this article show the appearances presented 65 hours and 6 days after the application of the oil (see Plate X). All the usual features of an accidental poisoning were reproduced in this case of intentional poisoning. Even the treatment applied for the first 8 days was such as is employed by expert dermatologists who have had a large experience of this peculiar dermatitis.

Besides Dr. Hibbard's case, I have produced two similar severe cases of dermatitis by means of the oil extracted from Rhus toxicodendron. In these two cases no medicine whatever was used. The eruption in these cases was just as severe, as was also the œdema, as in Dr. Hibbard's case. In these two cases spreading of the affection to other parts of the body was entirely prevented, simply by keeping the

* Loc. cit.

inoculated arm bandaged constantly. Changes of the bandage were not made by the inoculated person, but by other hands, so that a transfer of the poisonous oil from the inoculated forearm to other parts of the body of the same person was impossible.

To test the strength of the toxicodendrol and the latent period of the dermatitis, I made dozens of experiments upon myself and others, who kindly gave not only their assistance for these experiments, but also underwent the discomfort and pain which they entailed.

In all cases, without a single exception, the free purified toxicodendrol, obtained by decomposition of its lead compound, proved to be a very severe skin irritant. The minutest traces of it were active. The degree of activity varied, however, in different persons. In some 0.1 milligramme produced many hundreds of vesicles and considerable œdema of the forearm; in one person even $\frac{1}{100}$ mg. caused such a severe dermatitis that the whole forearm was extensively swollen and the pain so severe that sleep was impossible for a few nights. Even $\frac{1}{1000}$ mg. dissolved in two drops of olive oil proved to be active in one person. Severe itching, a few dozen of vesicles and localized œdema followed the application of that small dose.

The latent period varied, as in accidental poisoning, in wide limits. In some persons redness, swelling, itching, and even papules, were noticed from 18 to 24 hours after the application of the oil. In other cases 7 and even 9 days elapsed before the first symptoms were noticed. In most cases the first symptoms appeared four to five days after the application of the oil.*

The skin eruption may be produced also on rabbits, if the fur is cut short. In these animals the latent period seems to be longer, as the skin eruption makes its appearance, as a rule, in from one to even two weeks. Swelling, localized redness and the formation of papules, vesicles and crusts are well marked. The eruption, conforming to

* I may give here an interesting case of accidental poisoning showing the latent period of poison ivy. On a Tuesday three men were helping me to divide about 10 k. of freshly collected poison ivy. All these showed the following Sunday the first symptoms of poisoning. Neither before nor after this Tuesday had these persons been near poison ivy. In their case, therefore, the latent period was five days.

the non-volatility of the poison, remains perfectly localized, and only the tissue near the point of application undergoes pathological changes. The continued action of the toxicodendrol on the rabbit's skin is followed by an increase in length of the hairs of the spots affected, the fur, too, becoming more shiny. In the case of one dark rabbit the new hairs were of a lighter color.

Another well-known cutaneous irritant, cantharides, is used with some benefit in practical medicine as a hair restorer, where the pathological condition is due to a malnutrition of the skin. But it is not probable that toxicodendrol can act as a substitute for cantharides, as the great œdema caused by minute amounts of the oil will doubtless prevent its use for this purpose.

The effects on the system following an internal administration of toxicodendrol have been studied in a few rabbits. The oil was given to these animals either in alcoholic solution or dissolved in pure olive oil. These solutions were given *per os* through a stomach tube. The irritant properties of toxicodendrol were most marked on the kidneys, producing nephritis and conspicuous fatty degeneration of this organ. In one case the stomach of the animal was found to be the seat of extreme diphtheritis. The symptoms after internal administration of toxicodendrol to rabbits were complete loss of appetite, suppression of urine, and later albuminous urine (0.5 per mille albumin in one case), with blood corpuscles and renal epithelium. Some animals died shortly after administration of the oil. The autopsies revealed no cause of death in these cases, only slight redness of the mucous membrane of the stomach being observed.

The cases recorded in medical literature in which death has followed after severe poisoning with poison ivy may have been caused by renal complications. It is not impossible that these persons may have suffered previously from some chronic renal trouble, and after being poisoned with poison ivy or poison sumach, enough of the poisonous oil was absorbed from the skin to cause an acute exacerbation of the already existing disease of the kidney, and thus to lead to a fatal end.

This explanation is suggested merely as an hypothesis to explain the few fatal cases following poisoning with Rhus. Whether in fact

the recorded cases of fatal issue after poisoning with poison ivy had any real connection with these poisonous plants is open to doubt, as the history of these cases is open to criticism, and it is especially to be remarked that in not one case has an autopsy been made. The real cause of death may have been, therefore, entirely overlooked.

As to the rational treatment of Rhus poisoning, it is to be noted that the poisonous oil, as we have already repeatedly stated, is non-volatile. It is very sticky and will cling persistently to parts which may have become contaminated with it. It oxidizes in contact with air and is transformed into a solid resin. But this process is a very slow one. This resinification of the oil may be hastened by heat and alkalies, even by a solution of carbonate of sodium, but still the process remains a very slow one. The metallic compounds of the oil, after decomposition, leave again the oil with all its irritant properties. The poisonous oil is soluble in most of the common solvents and fatty substances, but is insoluble in water.

From all the chemical properties just enumerated, the rational indication in a case of Rhus dermatitis would be to get rid of the poisonous oil that may still be on the skin of the affected person as quickly as possible, no matter in what stage the eruption may be.

This can be done by vigorously washing the affected and exposed parts with soap, water and a scrubbing brush, that is to say, mechanically. As the active principle is very soluble in alcohol and gives with lead acetate a precipitate which is nearly insoluble in alcohol (the copper and iron compounds are also easily obtained as precipitates), other processes may be employed to remove the oil. The exposed parts may be washed repeatedly with fresh quantities of alcohol and a scrubbing brush. The poisonous oil would be thus removed in alcoholic solution; or still another way of operating would be to wash the exposed parts with an alcoholic solution of lead acetate. In this case the poisonous principle would be first transformed into its insoluble lead compound and then washed away with alcohol. The washing must be done thoroughly when alcohol is employed, as otherwise the alcohol would only help the spreading. The nails have to be cut short and also perfectly cleaned with the scrubbing brush. Oily

preparations, or anything which dissolves the poisonous oil, if used and not *immediately* removed, would only spread the poison, giving it a larger area on which to work. This spreading was well seen in Dr. Hibbard's case. The vaseline ointment used in the treatment dissolved the oil which adhered to the point of application, and thus caused the spreading of the eruption. That the proposed treatment does not cure the already inflamed parts is self-evident.

How can the commonly accepted idea be explained that poisoning may occur without actual contact with the poisonous plants when the active principle is a non-volatile substance?* The activity of toxicodendrol in minutest traces may make it possible for a few pollen grains of poison ivy to cause skin eruption; and the few cases of action at a distance, which are so often quoted, may conceivably be thus explained. But, in my opinion, it is more than doubtful if ever a case of ivy poisoning has occurred without direct contact with the plant or some article which has been in contact with the plant. The long latent period of the eruption in some cases may obviously render mistakes extremely easy as to the occasion when contact with the plant really occurred.

I wish to express my thanks to Dr. Hibbard and to the other gentlemen who kindly took an active part in the experiments made upon the action of toxicodendrol on the human skin.

DESCRIPTION OF PLATE X.

Photographs of arm, showing dermatitis produced by an oil extracted from Rhus venenata.

Fig. 1.—65 hours after application of the oil.

Fig. 2.—6 days after application of the oil.

*** I have used more than 25 k. of fresh poison ivy and a few k. of poison sumach. Hundreds of persons passed through the laboratory during the time that these plants were handled, extracted, distilled, etc. In not one single instance was a person poisoned who did not come into actual contact with the plant or the free oil.**

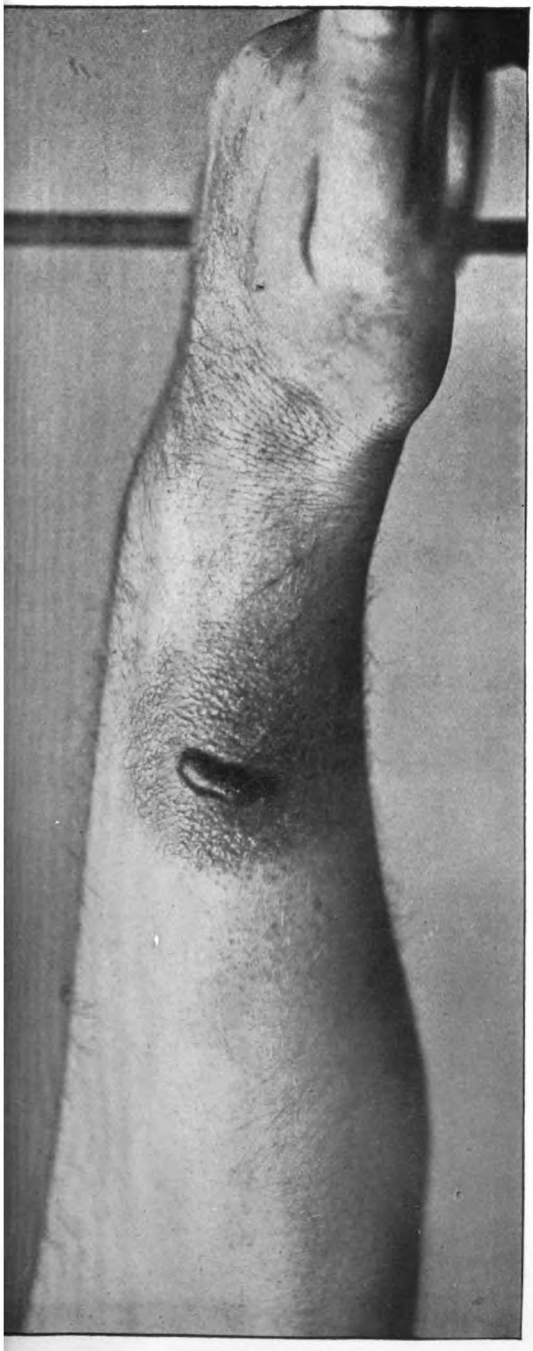

FIG. 1.

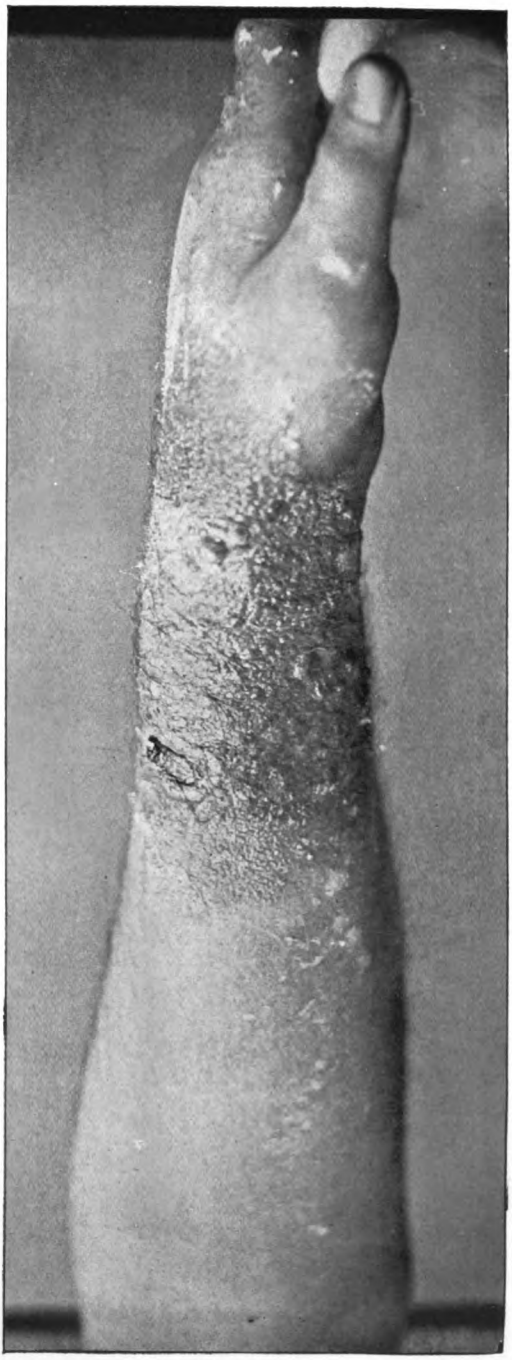

FIG. 2.